PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 730815	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. **PCT/SG2004/000353**	International filing date *(day/month/year)* 26 October 2004	Priority date *(day/month/year)* 27 October 2003

International Patent Classification (IPC) or national classification and IPC

Int. Cl. [7] C07C 275/50, 275/54, 311/58, 311/60, 335/26, C07D 209/14, 213/40, 233/61, 235/14, 285/06, 295/13, 295/215, 307/14, 307/85, 333/20, 333/38, 333/70, A61K 31/17, 31/341, 31/343, 31/44, 31/445, 31/381, 31/404, 31/433, 31/64, A61P 35/00

Applicant

S*BIO PTE LTD et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [X] *(sent to the applicant and to the International Bureau)* a total of 2 sheets, as follows:
      - [X] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      - [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

[X]	Box No. I	Basis of the report
[ ]	Box No. II	Priority
[X]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[X]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[ ]	Box No. VIII	Certain observations on the international application

Date of submission of the demand 18 July 2005	Date of completion of the report 23 September 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **S.R. IDRUS** Telephone No. (02) 6283 2659

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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

   [ ] international search (under Rules 12.3 and 23.1 (b))

   [ ] publication of the international application (under Rule 12.4)

   [ ] international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

   [ ] the international application as originally filed/furnished

   [X] the description:

   pages **1-3, 5-117** as originally filed/furnished
   pages* **4** received by this Authority on **18 July 2005** with the letter of **15 July 2005**
   pages* received by this Authority on with the letter of

   [X] the claims:

   pages **118, 120-140** as originally filed/furnished
   pages* as amended (together with any statement) under Article 19
   pages* **119** received by this Authority on **18 July 2005** with the letter of **15 July 2005**
   pages* received by this Authority on with the letter of

   [ ] the drawings:

   pages as originally filed/furnished
   pages* received by this Authority on with the letter of
   pages* received by this Authority on with the letter of

   [ ] a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. [ ] The amendments have resulted in the cancellation of:

   [ ] the description, pages
   [ ] the claims, Nos.
   [ ] the drawings, sheets/figs
   [ ] the sequence listing (*specify*):
   [ ] any table(s) related to the sequence listing (*specify*):

4. [ ] This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   [ ] the description, pages
   [ ] the claims, Nos.
   [ ] the drawings, sheets/figs
   [ ] the sequence listing (*specify*):
   [ ] any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos: **1-35 (in part)**

because:

☐ the said international application, or the said claims Nos.
relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos.
are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos.
are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claim Nos. **1-35 (in part)**

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	**1-79**	**YES**
	Claims		**NO**
Inventive step (IS)	Claims	**1-79**	**YES**
	Claims		**NO**
Industrial applicability (IA)	Claims	**1-79**	**YES**
	Claims		**NO**

2. Citations and explanations (Rule 70.7)

Where no international search report was established in respect of certain claims or parts thereof, the question whether the claimed invention is novel, involve inventive step and industrially applicable have not been examined.

For the search that was conducted, the International Search Report identified the following citations:

D1) STN File CA Abstract Accession No. 133:53160

D2) STN File CA Abstract Accession No. 132:342787

D3) Derwent Abstract Accession No. 2004-383257/36

D1 and **D2** are the closest prior-art and disclosed compounds which are excluded by Claims 1-15, and 18. As such there is no overlap between the subject matter disclosed in the prior art documents and the subject matter of the present claims. Moreover, there is no teaching or suggestion in **D1** and **D2** that the compounds of the prior art would be useful for the inhibition of histone deacetylase and, as such, could be used for the treatment of cancer.

Accordingly, the claimed subject matter are novel and involve inventive step in the light of **D1** and **D2**.

D3 is an intermediate document and is mentioned in Box VI.

The compounds of the present invention are inhibitors of histone deacetylase (HDACs) and it is understood that inhibition of HDACs will cause apoptosis of cancer cells. Thus the claimed subject matter has industrial applicability.

With regard to the document(s) listed in Box VI under "certain documents cited", these are documents published prior to the international filing date but later than the priority date claimed but which would otherwise be considered to be of particular relevance.

Under the PCT, novelty is considered only in respect of documents published before the priority date. The relevance of a document published after the priority date is dependent upon national law. Such documents are excluded from consideration in preliminary examination, under the PCT Guidelines but have been included here for information.

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Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
JP 2004143053 A ("X")	20 May 2004	22 October 2002	22 October 2002

This application disclosed compounds which fall within the scope of Claim 1-16, and 18 in the instances that G^1 is C=O which would be equivalent to M; L is G^2NH so that it's C(=O)NH wherein the C(=O) would be equivalent to the Q in present claims and R^2 is equivalent to G in present claims. This citation may therefore influence novelty of Claim 1-16, and 18.

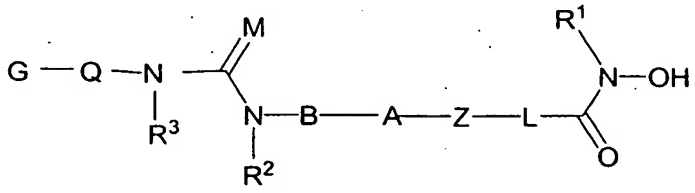
2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

heterocycloalkylalkyl, arylalkyl, heteroarylalkyl and acyl; each of which may be optionally substituted;

or a pharmaceutically acceptable salt or prodrug thereof, wherein when R is methyl or isopropyl methyl then R_2 is not benzyl.

In one preferred embodiment the present invention provides compounds having the Formula (2)



Formula (2)

wherein

R^1 is selected from the group consisting of H, C_1 -C_6 alkyl and acyl;

L is a single bond or is a C_1-C_5 hydrocarbon chain which may contain 0 to 2 multiple bonds independently selected from double bonds and triple bonds and wherein, the chain may optionally be interrupted by at least one of -O-, -S-, -S(O)- and -$S(O)_2$- and the chain may optionally be substituted with one or more substituents independently selected from the group consisting of C_1-C_4 alkyl;

Z is selected from the group consisting of a single bond, N(R^1), O, S, S(O) and $S(O)_2$;

A is selected from the group consisting of a single bond, optionally substituted arylene, optionally substituted heteroarylene, optionally substituted cycloalkylene and optionally substituted heterocycloalkylene;

B is selected from the group consisting of a single bond, optionally substituted aminoacyl, optionally substituted arylene, optionally substituted heteroarylene, optionally substituted arylalkylene, optionally substituted heteroarylalkylene, optionally substituted alkylarylene, optionally substituted alkylheteroarylene, optionally substituted C_1-C_3 alkylene, optionally substituted heteroalkylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene and optionally substituted -$(CH_2)_m$-C(O)-N(R^4)-$(CH_2)_n$-, wherein n is an integer from 0 to 6, m is an integer from 0 to 6;

heteroaryloxy, arylalkyloxy, amino, alkylamino, aminoalkyl, acylamino, arylamino, sulfonylamino, sulfinylamino, phenoxy, benzyloxy, $COOR^4$, $CONHR^4$, $NHCOR^4$, $NHCOOR^4$, $NHCONHR^4$, $C(=NOH)R^4$, alkoxycarbonyl, alkylaminocarbonyl, sulfonyl, alkylsulfonyl, alkylsulfinyl, arylsulfonyl, arylsulfinyl, aminosulfonyl, aminosulfinyl, SR^4 and acyl; each of which may optionally be substituted;

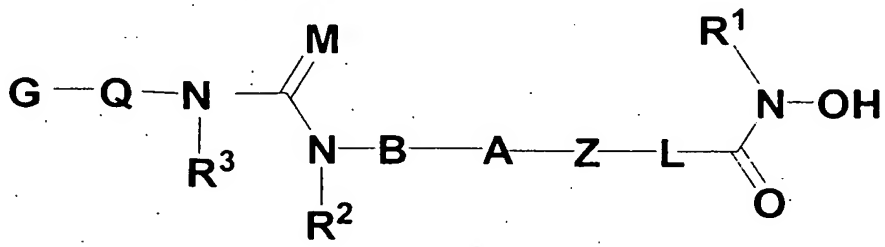
Q is selected from the group consisting of $-S(O)_2-$, -C(=O)- and –C(=S)-;

G is selected from the group consisting of optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, optionally substituted arylalkyl, and optionally substituted heteroarylalkyl;

each R^4 is independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, heteroarylalkyl and acyl, each of which may be optionally substituted;

or a pharmaceutically acceptable salt or prodrug thereof, wherein when R is methyl or isopropyl methyl then R_2 is not benzyl.

2. A compound according to claim 1 having the Formula (2)



Formula (2)

wherein

R^1 is selected from the group consisting of H, C_1 -C_6 alkyl and acyl;

L is a single bond or is a C_1-C_5 hydrocarbon chain which may contain 0 to 2 multiple bonds independently selected from double bonds and triple bonds and wherein, the chain may optionally be interrupted by at least one of -O-, -S-, -S(O)- and $-S(O)_2-$ and the chain may optionally be substituted with one or more substituents independently selected from the group consisting of C_1-C_4 alkyl;